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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/691,468	10/22/2003	Stephen C. Strom	12958/46103	5954

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Deborah A. Somerville
KENYON & KENYON
One Broadway
New York, NY 10004

EXAMINER	
NGUYEN, QUANG	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 06/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/691,468	STROM ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-7,9-14,16-21,23-28,30-35 and 37-61* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-43,46-50,53 and 54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/14/04;7/25/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 5-7,9-14,16-21,23-28,30-35,37-39,44,45,51,52 and 55-61.

DETAILED ACTION

Applicant's election of Group I in the reply filed on 5/11/06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants further elected SSEA-4 as a species of a cellular marker.

Claims 5-7, 9-14, 16-21, 23-28, 30-35, 37-61 are pending in the present application. Claims 5-7, 9-14, 16-21, 23-28, 30-35, 37-39 and 55-61 were withdrawn. Claims 44-45 and 51-52 were also withdrawn because they are directed to non-elected species.

Accordingly, claims 40-43, 46-50 and 53-54 are examined on the merits herein with SSEA-4 as the elected species of a cellular marker.

Specification

The disclosure is objected to because certain paragraphs contain blanks to be filled in (see at least pages 5-7, 10 and 15-18).

Appropriate correction is required.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 40-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116.

Applicant's invention is drawn to a composition comprising a placental stem cell isolated from the amnion or from the amniotic epithelium, wherein the composition is enriched for cells that express at least one marker selected from a Markush group recited in either claim 40 or claim 42 with SSEA-4 as the elected maker; and a pharmaceutical composition comprising the same.

Apart from the disclosure that a cell population that is obtained from a placental tissue contains cells expressing various stem cell markers, epithelial cell markers and hepatocyte markers, the instant specification fails to describe sufficiently the characteristics and/or essential features possessed by an isolated "placental stem cell". For example, what are the structural characteristics or cellular markers possessed by a placental stem cell isolated from the amnion or from the amniotic epithelium? Are these

placental stem cells the same or different? If they are different, then in which ways? It is further noted that there is no single cellular marker that is specific for any given cell type, for this instance a placental stem cell isolated from either the amnion or the amniotic epithelium. Applicants also fail to provide a representative number of species for a broad genus of a placental stem cell in the compositions as claimed.

The claimed invention as a whole is not adequately described. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention: Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a placental stem isolated from either the amnion or the amniotic epithelium present in the compositions as claimed, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 40-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In independent claims 40 and 42, the metes and bounds of the claims are not clearly determined because it is unclear what is the relationship between a placental stem cell isolated from the amnion or from the amniotic epithelium with cells that express at least one marker recited in the Markush group of claim 40 or 42. Is the placental stem cell the same or different from cells expressing at least one of the recited markers?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 40-43, 46-50 and 53-54 are rejected under 35 U.S.C. 102(b) as being anticipated by Hu et al. (WO/73421 A2; IDS).

With respect to claims 40-43, the examiner interprets a placental stem cell isolated from the amnion or from the aminotic epithelium as a cell that also expresses at least one marker from the Markush group in claim 40 or claim 42, with SSEA-4 as the elected cell marker.

Hu et al disclosed the isolation of pure multipotential human amniotic epithelial cells obtained from separated amnionic membrane of a placenta at delivery (see abstract, and examples 1-2). The isolated amniotic epithelial cells are characterized by round, cobblestone morphology, large nuclei, epithelial membrane antigen and cytokeratin staining and gap junctional communication (page 6, lines 13-15). Additionally, Hu et al teach that that the isolated amniotic epithelial cells can be cultured in various media, such as DMEM, F-12, M199, RPMI and combinations thereof, supplemented with fetal bovine serum (FBS), whole human serum (WHS), or human umbilical cord serum or supplemented with growth factors, cytokines, hormones, vitamins, or any combinations thereof (page 6, lines 16-21). Specifically, the isolated amniotic epithelial cells may be induced to differentiate with various epithelial differentiation-inducing agents such as growth factors (e.g., EGF, aFGF, bFGF, PDGF, TGF-beta), hormones (e.g., insulin, triiodothryonine, hydrocortisone, dexamethasone), cytokines (IL-1, IFN-gamma, TFN), retinoic acid, transferrin, TPA and DMSO (page 8, lines 13-20). Alternatively, the isolated amniotic epithelial cells may also be expanded in the presence of an agent that suppresses cellular differentiation such as leukemia

inhibitory factor (LIF) and stem cell factor (page 6, line 27 continues to line 2 of claim 7). Hu et al also teach that the isolated human amniotic epithelial cells are used as autologous/heterologous tissue regeneration/replacement therapy at least for cartilage repair, facial dermabrasion, burn and wound dressing for traumatic injuries of skin (page 9, lines 18-24) as well as in reconstructive treatment of damaged tissue by surgical implantation of cell sheets, disaggregated cells, and cells embedded in carriers for regeneration of tissues for which differentiated cells have been produced (page 9, line 25 continues to line 2 of page 10).

Since the multipotential human amniotic epithelial cells of Hu et al. are derived from the same tissue source, and that they are isolated by a similar method, and in light of their disclosed characteristics, it is inherent that these multipotential human amniotic epithelial cells also possess the SSEA-4 cell marker and other characteristics of the compositions as claimed. Please, also note that where, as here, the claimed and prior art products are identical **or** substantially identical, or are produced by identical **or** substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke. Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Accordingly, Hu et al anticipate the instant claims.

Claims 40-43, 46-50 and 53-54 are rejected under 35 U.S.C. 102(e) as being anticipated by Atala et al. (WO 03/042405 A2; IDS).

Atala et al disclosed the isolation of pluripotent fetal stem cells derived from chorinonic villus, amniotic fluid and placenta (see Summary of the Invention, pages 2-5). These pluripotent fetal stem cells were of epithelial origin, stained positive for cytokeratins, *c-kit*, CD34, AC133, SSAE3, SSAE4 and possess telomerase activity (see paragraphs 98, 100-101 and 106). Atala et al also disclose that these fetal stem cells are capable of differentiating to cells of different lineages, including but not limiting to osteogenic, adipogenic, myogenic, neurogenic, hematopoietic and endothelial lineages (at least paragraph 11). Atala et al also teach that the purified or enriched fetal stem cell populations can be cultured in various media such as DMEM, F-12, MI 99, RPMI and combinations thereof, or supplemented with growth factors, cytokines, hormones, vitamins, antibiotics, or any combination thereof (paragraph 80). The stem cells can be cultured in the presence of agents such as keratinocyte growth factor, EGF, aFGF, bFGF, PIDGF, TGF-P, insulin, prolactin, cytokines, retinoic acid and others to induce differentiation (paragraphs 81 and 83). Atala et al further teach that the fetal stem cells can be used as autologous/heterologous tissue regeneration/replacement therapy, including at least for cartilage repair, corneal epithelial defects, facial dermabrasion, burn and wound dressing for traumatic injuries of skin, mucosal membranes and others (paragraph 87). Additionally, the fetal stem cells can also be embedded in carriers for

regeneration of tissues for which differentiated cells have been produced (paragraph 88).

Please, also note that where, as here, the claimed and prior art products are identical **or** substantially identical, or are produced by identical **or** substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke. Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Accordingly, Atala et al anticipate the instant claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 40-43, 46-50 and 53-54 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 26-36 and 38-50 of copending Application No. 10/420,656.

Although the conflicting claims are not identical, they are not patentably distinct from each other because a composition comprising or enriched for a non-tumorigenic amniotic epithelial cell which expresses at least one marker selected from the group consisting of: c-kit, Thy-1, OCT-4, SOX2, hTERT, SSEA1, SSEA3, SSEA4, TRA1-60 and TRA-81 in the co-pending Application No. 10/420,656 contain species that anticipate the claimed genus of a composition in the application being examined and, therefore, a patent to the genus would, necessarily, extend the rights of the species or sub-, should the genus issue as a patent after the species of sub-genus.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 40-43, 46-50 and 53-54 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2, 9-13, 20-21 of copending Application No. 10/577,024.

Although the conflicting claims are not identical, they are not patentably distinct from each other because a composition comprising a placental stem cell isolated from the amnion or from the amniotic epithelium and enriched for cells that express at least

one marker from the group consisting of: c-kit, Thy-1, OCT-4, Nanog, SOX2, SSEA3, SSEA4, TRA1-60, TRA-81, Lefty A, FGF-4, Rex-1 and TDGF-1, a pharmaceutical composition comprising the same composition, and a composition comprising a cultured proliferating placental stem cell isolated from the amnion which expresses at least one marker selected from the group consisting of c-kit, Thy-1, OCT-4, Nanog, SOX2, SSEA3, SSEA4, TRA1-60, TRA-81, Lefty A, FGF-4, Rex-1 and TDGF-1 in the co-pending Application No. 10/577,024 contain species that anticipate the claimed genus of a composition in the application being examined and, therefore, a patent to the genus would, necessarily, extend the rights of the species or sub-, should the genus issue as a patent after the species of sub-genus.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusions

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Dave Nguyen, may be reached at (571) 272-0731.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

QUANG NGUYEN, PH.D
PATENT EXAMINER